REMARKS

The specification has been amended to correct an obvious error at page 26. Claims 1-46 have been canceled. New claims 47-63 have been added. The new claims are supported throughout the application, e.g., at page 3, lines 19-21; page 4, lines 5-6 and 24-25; page 13, lines 37-39; page18, lines 5-8; page 26, lines 1-10, and by the original claims as filed. No new matter has been added.

In the office action mailed March 20, 2001, the previously pending claims were rejected as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In particular, the Examiner offered the following grounds for the rejection.

> Applicant argues at page 8 of the response that the specification identifies "the structure of peptides useful as MCH antagonists and the structure of critical residues." This argument is not persuasive because the specification provides conflicting information as to what would constitute an antagonist versus an agonist. Furthermore, the assertion of antagonistic activity is not founded on experimental data but rather, on salmon MCH activity in teleost skin bioassay and frog and lizard bioassay models. The evidence does not establish that these assays and models are effective for predicting MCH mutants which will function as antagonists, absent evidence to the contrary.
> ***
> Therefore, the specification does not provide clear guidance as to which amino acids (i.e., structural elements) of the native protein are critical to the biological activity of an antagonist and which amino acids should be altered in order to obtain an MCH antagonist.

The rejection is respectfully traversed. The present claims are directed to a method of inhibiting appetite or weight gain. The method includes administering an effective amount of an antagonist of MCH to a subject, wherein the antagonist binds an MCH receptor. Applicants submit herewith a declaration under 37 C.F.R. § 1.132 of Dr. Eleftheria Maratos-Flier, setting forth evidence that the presently pending claims are enabled.

As stated in Dr. Maratos-Flier's declaration, the results obtained from the skin bioassays described in the application are indeed sufficiently predictive of the structure-function relationship of MCH to determine what MCH analogs would act as antagonists. The specification teaches particular regions of MCH that can be mutated to make antagonists and teaches various assays for following activity, including *in vitro* and *in vivo* assays for antagonist activity. For example, the specification teaches that the MCH ring structure is important for MCH activity and can be mutated in an antagonist. The results described in the specification (and the predictions made from the results about MCH activity) have been essentially confirmed by other investigators, e.g., by Audinot et al. (2001) J. Biol. Chem. 276:13554-13562 (copy enclosed). Audinot et al. (which was published after the priority date of the present application) made mutant peptide analogs of MCH and tested the mutant peptides for activity against a human cell transfected with a human MCH receptor. Using this assay system, Audinot et al. found numerous antagonists (8 of 57 mutant peptides made). All of the antagonists included changes in the MCH ring structure, which is taught by the specification to be important for MCH activity.

Further, the specification provides sufficient guidance for a skilled artisan to make and use non-peptide antagonists of MCH that bind an MCH receptor as well. Using methods such as those provided in the specification or very similar methods, other investigators have been able to identify MCH antagonists that bind competitively to the MCH receptor and perform the claimed methods. For example, Takekawa et al. (2002) European J. Pharmacol. 438:129-135 (copy enclosed) used a combination of *in vitro* and *in vivo* testing, very similar to the methods taught in the specification, to identify the MCH antagonist T-226296, a (-) enantiomer of N-[6-(dimethylamino)-methyl]-5,6,7,8-tetrahydro-2-naphthalenyl]-4'-fluoro[1,1'-biphenyl]-4-carboxamide, from a library of chemical compounds.

Accordingly, as evidenced by the enclosed declaration of Dr. Maratos-Flier, one of ordinary skill in the art could perform the claimed methods using the knowledge in the art and the guidance provided in the specification.

Applicant asks that all claims be allowed. A Petition for Extension of Time along with the required fee is enclosed. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing the attorney docket number indicated above.

Respectfully submitted,

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for: Leda Lucivero, Reg. No. 50,635
Louis Myers
Reg. No. 35,965

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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Version with markings to show changes made

In the specification:

Paragraph beginning at page 26, line 1-6 has been amended as follows:

In preferred embodiments: the antagonist has a disulfide bridge between residues R^7 and R^{16}; the disulfide ring includes ten amino acids; the antagonist is deleted for any or all of the residues between R^1 and R^6; the antagonist is deleted for one or both of the residues between R^{18} and R^{19}; the antagonist has at least 70, 80, or 90% homology with human, rat or salmon MCH; the [agonist] antagonist has 1, 2, 3, 4, 5 or more residues within the ring modified or substituted with a nonconserved amino acid.